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ANNUAL PROGRESS REPORT

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Dr. James G. Fujimoto and Dr. Mark Brezinski

INSTITUTION:

Massachusetts Institute of Technology and  
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Optical Coherence Tomographic Imaging and Delivery for  
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**OBJECTIVE:** The objective of this program is to develop and apply optical coherence tomography (OCT) for biomedical applications. OCT is a new technology for performing in situ, real time imaging of cross sectional tissue microstructure. This program explores OCT technology and its applications for surgical guidance and optical biopsy.

**APPROACH:** This program is an ongoing collaboration between investigators at the Massachusetts Institute of Technology, the Massachusetts General Hospital, and the Harvard Medical School. The program includes both technology development and biomedical studies. Optical Coherence Tomography (OCT) is a new imaging technology which was previously developed in part under this program. OCT is analogous to ultrasound imaging except that it uses light instead of sound. OCT produces cross sectional images of tissue with micron scale resolution by measuring the echo time delay and magnitude of backscattered light. OCT can generate high resolution (1-15  $\mu\text{m}$  resolution) cross sectional images of tissue microstructure in situ and in real time. OCT can function as a type of optical biopsy to provide information which is analogous to conventional biopsy and pathology, but without the need to remove and process a specimen. Our program spans several complementary components: development of new laser sources for imaging; optical systems technology and measurement techniques for optical coherence tomography and imaging; fundamental studies of tissue optical and spectroscopic properties; studies of pathology in vitro to establish the feasibility of using OCT in surgical guidance and early neoplastic diagnosis; and preliminary clinical studies.

ACCOMPLISHMENTS (last 12 months):

Ultrahigh resolution and spectroscopic optical coherence tomography imaging We have recently demonstrated ultrahigh resolution OCT imaging with axial resolutions of  $\sim 1 \mu\text{m}$ , the highest resolutions achieved to date. These results were made possible using novel ultrashort pulse laser technology developed synergistically under our ongoing AFOSR photonics program. We have developed a short pulse  $\text{Ti:Al}_2\text{O}_3$  laser which generates pulse duration of  $\sim 5 \text{ fs}$  or 2 cycles of light, spanning the wavelength range from  $\sim 650\text{-}1000 \text{ nm}$ . These extremely broad bandwidths enable ultrahigh resolution as well as spectroscopic OCT imaging. We have developed spectroscopic OCT techniques which permit spectral imaging across the near IR with micron scale resolution. These techniques promise to enable functional imaging of tissue by detecting the spectroscopic signatures of properties such as oxygenation or blood flow.

New imaging technology In addition to ultrahigh resolution and spectroscopic OCT, we have developed a portable, high speed OCT imaging system suitable for performing preliminary clinical OCT imaging studies. Our portable system can perform imaging at 8 frames per second with axial resolutions of  $10\text{-}15 \mu\text{m}$ . One of the advantages of OCT imaging is that since it is fiber optically based, it can be interfaced to a wide range of delivery systems. We have integrated OCT with ophthalmoscopes and surgical microscopes, colposcopes, hand held imaging probes, as well as catheter and endoscopic devices which enable internal body imaging.

Studies in biological systems Ultrahigh resolution imaging studies have been performed in a wide range of biological tissues both in vitro and in vivo. In vitro studies have focused on establishing the correspondence of OCT imaging to histology. Studies have been performed on cancers of the gastrointestinal tract, female reproductive tract (including ovarian, uterine, and cervical neoplasia), and prostate cancer. OCT has been investigated for real time imaging in surgical guidance on in vitro models including RF and laser ablation as well as microsurgery.

Preliminary clinical imaging studies We have begun preliminary studies in patients to investigate OCT imaging in a variety of different clinical areas. Working in collaboration with Dr. S. Martin at the Veterans Administration Hospital and Harvard Medical School, we are investigating OCT imaging for detecting early arthritic changes. OCT has been demonstrated to differentiate normal versus abnormal cartilage during open field knee replacement surgery. Working in collaboration with Drs. J. Van Dam from the Brigham and Women's Hospital and Harvard Medical School, and H. Mashimo from the VA Hospital, we have begun endoscopic imaging studies of the upper gastrointestinal tract. These studies investigate the ability of OCT to image early neoplastic changes. Working with Dr. A. Goodman of the Massachusetts General Hospital, we have demonstrated OCT imaging of the cervix. The cervix is an important model system for investigating imaging of neoplasia. Working with Dr. J. Beamis of the Lahey Clinic, we are beginning bronchoscopic imaging studies of lung cancer and dysplasia. Taken together, these studies should yield important information on clinical applications of OCT.

Ophthalmic Imaging Preliminary ultrahigh resolution imaging studies of the human retina and anterior eye have also been performed. Image resolutions of 3  $\mu\text{m}$  have been demonstrated, limited by the chromatic aberration of the lens. These represent a factor of 4 to 5 improvement over the 10-15  $\mu\text{m}$  resolution retinal images performed with previous systems. The improvement in image resolution and quality permits internal retinal features to be visualized for the first time and improves the accuracy of quantitative measurement of the retina and retinal nerve fiber layer thickness. These studies are relevant for the early diagnosis of glaucoma or diabetic retinopathy.

Technology transfer In 1998 we transferred OCT technology to a start-up company, Coherent Diagnostic Technology. This company licensed intellectual property from the Massachusetts Institute of Technology and is commercializing OCT technology for clinical applications in internal body imaging. In 1992 OCT technology for ophthalmic diagnostics was transferred to Humphrey Systems. Humphrey developed an ophthalmic retinal diagnostic device which was introduced commercially in 1996. The availability of this technology enabled extensive clinical studies in ophthalmology to be performed. A second generation ophthalmic OCT product line is currently being developed. This second generation technology is intended for use by the general ophthalmologist and promises to become a widespread tool for clinical ophthalmology.

SIGNIFICANCE: The development of techniques for optical biopsy, the in situ, real time imaging of tissue microstructure, are important for a variety of clinical situations where conventional excisional biopsy is hazardous or impossible, where excisional biopsy suffers from sampling errors yielding an unacceptable false negative rate, and for guiding surgical intervention. OCT is a fundamentally new imaging modality which could have a widespread impact in a wide range of medical disciplines including ophthalmology, cardiology, gastroenterology, gynecology, orthopedics, and surgery.

WORK PLAN: We will continue technology research to develop new high resolution, high speed OCT imaging and delivery. Special emphasis will be placed on spectroscopic imaging techniques and methods for performing functional imaging. Continuing studies on model systems will be performed to develop concepts for surgical guidance including microsurgery and tumor excision. Preliminary feasibility studies on OCT imaging in patients will be performed in the areas of orthopedics, gastroenterology, pulmonology, and gynecology.

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